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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,748	06/18/2001	Kunio Shiota	04853.0074	8762

22852 7590 12/24/2003

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER  
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WASHINGTON, DC 20005

EXAMINER
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BRUSCA, JOHN S

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/881,748

Applicant(s)

SHIOTA ET AL.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 November 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 4-14 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 5-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Newly submitted claim 14 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 14 is drawn to a method of making differentiated cells by methylating or demethylating gene regions, while the elected invention is drawn to a method of comparison of the methylation pattern of the DNA of cells.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 14 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. In the applicant's remarks filed 06 November 2003 the applicants state that claim 14 should be examined as part of the elected invention because examination of claim 14 does not require an additional search burden since it is drawn to a method of use of the gene regions identified in claim 7, however the search for claim 14 is not coextensive with claim 7 since claim 14 requires modification of methylation patterns in living cells.

### ***Claim Rejections - 35 USC § 112***

3. The rejection of claim 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 07 August 2003 is withdrawn in view of the amendment to claim 5 filed 06 November 2003.

### ***Claim Rejections - 35 USC § 102***

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4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 5, 7, and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Duffy.

The claims are drawn to a method of comparison of DNA methylation patterns of different cells. In some embodiments the comparison serves to identify the type or differentiation state of cells, and the methylation patterns are in gene regions.

Duffy shows in the abstract a method of comparison of DNA methylation patterns of cells. In some embodiments the methylation pattern is at a coding or regulatory region of a gene. In some embodiments the method is used as a diagnostic test to determine cancerous cell types. Duffy provides guidance in column 11 to use cells that are cancer cells, and to compare such cells with normal type cells from analogous tissues. Duffy provides working examples of their method in columns 21-28.

6. Claims 1, 5-7, 9-11, and 13 rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al.

The claims are drawn to a method of comparison of DNA methylation patterns of different cells. In some embodiments the comparison serves to identify the type or differentiation state of cells, or the methylation patterns are in gene regions. In some embodiments at least 1,000 gene regions are examined, or analysis is performed by restriction landmark genomic scanning.

Zhu et al. shows in column two of page 8058 that they performed a restriction landmark genomic scanning analysis of human T cells. Zhu et al. shows that the analysis was done in a

manner allowing for detection of methylation patterns of genomic DNA. Zhu et al. details their methodology on page 8059. Zhu et al. shows analysis of 1,068 fragments for methylation differences on page 8059. Zhu et al. correlate methylation differences detected by their method with types or differentiation states of the T cell lineages examined, for example in Table 3.

7. Claims 1, 5, 7, 8, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Hertz et al.

The claims are drawn to a method of comparison of DNA methylation patterns of different cells. In some embodiments the comparison serves to identify the type or differentiation state of cells, and the methylation patterns are in gene regions. In some embodiments the cells are stem cells.

Hertz et al. shows in the abstract the assay of methylation patterns of genes in several different mouse embryonic stem cell lines. The differences of methylation patterns in inserted genes are detailed in figures 4-9.

8. Applicant's arguments filed 06 November 2003 have been fully considered but they are not persuasive. The applicants state that Duffy does not show determination of patterns of methylation of different cells. Duffy determines the differences between patterns of methylation of two tested cells and therefore results in determination of the pattern of methylation of each of the tested cells. The claims are interpreted to read on the simultaneous comparison and detection of methylation patterns of Duffy.

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### ***Conclusion***

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

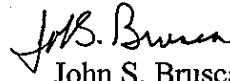
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 703 308-4231. The examiner can normally be reached on M-F 8:30-5:00. On approximately 12 January 2004 Art Unit 1631 will move to the new USPTO Alexandria, VA facility. At that time the phone number of the examiner will change to (571) 272-0714. Phone calls to the previous phone number will be referred to the new phone number for 60 days after the move date.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703 308-4028. The fax phone number for the organization where this application or proceeding is assigned is 703 872-9306.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

  
John S. Brusca  
Primary Examiner  
Art Unit 1631

jsb